

Laudatio for Jean-Laurent Casanova

by Prof. Dr. Jules A. Hoffmann

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Jean Laurent Casanova, MD and PhD, is a Professor and Head of Laboratory at the Rockefeller University. He is also a Senior Attending Physician at the Rockefeller University Hospital and an Investigator of the Howard Hughes Medical Institute. Jean-Laurent started his scientific career at the Necker Hospital and School of Medicine in Paris, as a Clinical and Research Fellow in the Pediatric Immunology Unit and Associated Laboratory, headed by Dr Claude Griscelli and subsequently Dr Alain Fischer. From 1999 to 2008 he was a Professor of Pediatrics in this Hospital and the Paris Descartes University, while building up his own laboratory devoted to Human Genetics of Infectious Diseases. In 2008 he moved to Rockefeller University, while keeping, as a Visiting Professor and Head of Laboratory, his close collaboration with the Necker Hospital and with his long-time associate, Dr Laurent Abel.

A pediatrician and an immunologist by training, Jean-Laurent Casanova centered his research interests over the years on human genetics, and more specifically, on the investigation of the immunological basis of life-threatening infectious diseases in children.

Dr Casanova recalls that his research in the field of human immunogenetics started with a simple question: *What are the reasons that lead some children to develop a severe clinical illness in the course of a primary infection while others exposed to the same microbe remain unharmed?* In a remarkable series of discoveries, Dr Casanova and associates were able to demonstrate that single-gene lesions in children can confer selective vulnerability to certain types of infections. Over the last twenty-five years, Dr Casanova has thus identified single-gene mutations underlying mycobacterial diseases, herpes simplex encephalitis, chronic mucocutaneous candidiasis and Kaposi sarcoma. The discovery of these simple genetic etiologies led Dr Casanova to decipher the molecular and cellular bases of the corresponding diseases. In this process Casanova and colleagues made major contributions to fundamental immunology in general and to characterization of pathways involved in given types of microbial infections. The results have also resulted in a paradigm shift in the field by pointing to the large redundancy of the immunological circuits in the context of human infections,

which had not been anticipated based on previous or parallel experimental studies in rodents.

Of major interest in the context of the Robert Koch prize is the fact that the studies of Jean-Laurent Casanova have already revolutionized the fight against some types of infections in affected children, by introducing specific treatments allowing the restoration of deficient immune responses (e.g. children with impaired IFN- production now benefit from IFN-therapy, and children with chronic mucocutaneous candidiasis can be relieved by administration of G-CSF and GM-CSF, which are normally induced by IL-17 cytokines). The new results also offer better molecular diagnosis and genetic counseling to families.

Beyond the cases of immune-deficient children studied by Jean-Laurent Casanova, his discoveries have also provided therapeutic openings in various acquired conditions, such as AIDS. The pathogenesis of chronic mucocutaneous candidiasis was initially attributed to an ill-defined T cell deficit. The identification of children with inborn errors of IL-17 immunity now points to the responsibility of this cytokine and warrants treatment with this molecule or its target molecules, such as G-CSF.

The identification and characterization of a significant number of genetic defects that predispose otherwise healthy children and young adults to a single type of infection by Dr Casanova and associates, have clearly opened a new field both in pediatrics and in immunology. They have also contributed to a better understanding of the pathways that govern the defenses against microorganisms. Last, but not least, they have provided some unexpected new avenues for curing or at least alleviating the conditions in the affected children.

Dr Casanova is the author or co-author of more than 300 papers, mostly in first class journals. He has created extremely efficient world networks of collaborations on pediatric diseases. He has already received numerous awards and distinctions and is a keynote speaker in all major meetings in the field. He has absolutely the perfect profile for a Koch Prize laureate!